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Way, Gaithersburg, MD 20878 (US). OSORIO, Manuel [US/US]; 4710 Bethesda Avenue #706, Bethesda, MD 20814 (US).

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(74) Agents: FANG, Carol, A. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111 (US).

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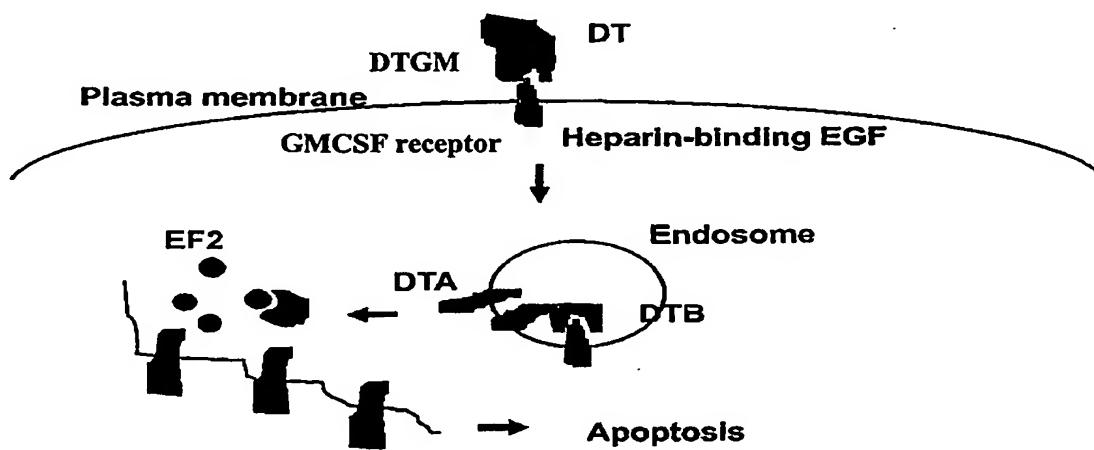
(71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES, as represented by THE SECRETARY OF HEALTH AND HUMAN SERVICES [US/US]; National Institute of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3804 (US).

(72) Inventors; and

[Continued on next page]

(75) Inventors/Applicants (for US only): LEPPA, Stephen, H. [US/US]; 9501 Starmont Road, Bethesda, MD 20817 (US). AVALONE, Jennifer [US/US]; 4 Beehive Lane, Flemington, NJ 08822 (US). BUGGE, Thomas [DK/US]; 9802 Bristol Square Lane, Apt. 302, Bethesda, MD 20814 (US). LIU, Shi-Hui [CN/US]; 14516 Settlers Landing

(54) Title: ACTIVATION OF RECOMBINANT Diphtheria TOXIN FUSION PROTEINS BY SPECIFIC PROTEASES HIGHLY EXPRESSED ON THE SURFACE OF TUMOR CELLS



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(57) Abstract: The present invention provides compositions and methods for inhibiting abnormal cell growth. In particular, the invention provides nucleic acids encoding Diphtheria toxin fusion proteins comprising residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has been substituted for a matrix metalloproteinase or plasminogen activator cleavage site, and a heterologous polypeptide and the polypeptides encoded by such nucleic acids. In addition, the invention provides methods of treating cancer by administering such polypeptides.

**Published:**

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/34 C12N15/62 A61P35/00 A61P35/02 A61K38/19
C07K14/535

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>LIU S ET AL: "Targeting of tumor cells by cell surface urokinase plasminogen activator-dependent anthrax toxin" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 276, no. 21, 25 May 2001 (2001-05-25), pages 17976-17984, XP002974279 ISSN: 0021-9258 cited in the application the whole document</p> <p>-----</p> <p style="text-align: center;">-/-</p>	1-49

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
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- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

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07/01/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Sommerfeld, T

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014306

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LIU SHIHUI ET AL: "Tumor cell-selective cytotoxicity of matrix metalloproteinase-activating anthrax toxin" CANCER RESEARCH, vol. 60, no. 21, 1 November 2000 (2000-11-01), pages 6061-6067, XP002311242 ISSN: 0008-5472 cited in the application the whole document	1-49
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014306

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	ABI-HABIB RALPH J ET AL: "A urokinase-activated recombinant diphtheria toxin targeting the granulocyte-macrophage colony-stimulating factor receptor is selectively cytotoxic to human acute myeloid leukemia blasts." BLOOD. 1 OCT 2004, vol. 104, no. 7, 1 October 2004 (2004-10-01), pages 2143-2148, XP002311244 ISSN: 0006-4971 -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/014306

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 24-48 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/US2004/014306

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